REMARKS

Claims 1-22 are pending in the present application. Claims 8, 9 and 13-22 have been withdrawn from consideration.

Pursuant to 37 C.F.R. §1.78(a)(2), the specification has been amended to add a paragraph containing a reference to U.S. Application No. 09/540,967, to which the present application claims priority. This priority information was included in the application transmittal sheet accompanying the originally filed application on January 2, 2002 and has already been noted by the Office, as indicated by the filing receipt of May February 8. 2002. As indicated by Federal Register Volume 66, No. 249, page 67089, second column, first full paragraph (published December 28, 2001),

> [i]f an applicant includes a claim to the benefit of a prior-filed nonprovisional application or international application designating the United States elsewhere in the application but not in the manner specified in §1.78(a)(2)(i) and (iii) (e.g., if the claim is included in an unexecuted oath or declaration or the application transmittal sheet) within the time period set forth in §1.78(a)(2)(ii), the Office will not require a petition (and the surcharge under §1.17(t)) to correct the claim if the information concerning the claim contained elsewhere in the application was recognized by the Office as shown by its inclusion on a filing receipt.

Accordingly, Applicants have not included a petition and accompanying surcharge with the present amendment to the specification that adds a paragraph referring to the claim of priority to U.S. Patent Application No. 09/540,967.

Objections to the Specification

The specification was objected to for not supplying the accession number of the hybridoma producing E4B9. The specification has been amended to include this accession number and Applicants request withdrawal of the objection.

The specification was also objected to for allegedly missing information. Specifically, the Examiner indicated that several monoclonal antibodies are labeled with asterisks in Figure 8 but there is nothing in the accompanying description in the specification indicating what these asterisks symbolize. A replacement drawing of Figure 8 has been submitted deleting these asterisks. Accordingly, Applicants request withdrawal of this objection.

The specification was also objected to for reciting amino acid sequences in Figures 2 and 9 in the absence of the appropriate sequence identifiers. Replacement drawings of Figures 2 and 9 have been submitted to include sequence identifiers. A substitute sequence listing in written form, a diskette containing the same sequence listing in computer readable format, and a sequence statement under 37 C.F.R.1.821 (f) and (g) is attached herewith. As such, Applicants submit that the sequence listing requirements as required by 37 C.F.R. 1.821-1.825 have been satisfied and Applicants request withdrawal of this objection.

The specification was also objected to for reciting "10G4" in the specification on page 23, line 21 but not identifying 10G4 in Figure 3. Applicants have amended the specification to refer to antibody 19E6, which is referred to in Figure 3.

Objections to the Claims

Claim 12 was objected to for referring to non-elected claims. Claim 12 has been amended and Applicants request withdrawal of this objection.

Rejection of Claims Under 35 U.S.C. 101

Claims 1-5 and 12 were rejected for allegedly not distinguishing over antibodies as they exist in nature. Claim 1 has been amended to recite that the antibody is "isolated." Applicants submit that this rejection has been overcome and request withdrawal of this rejection.

Rejection of Claims Under 35 U.S.C. 112, second paragraph

Claims 1-6 and 10-12 were rejected for being indefinite with respect to the recitation of "within the about 15 N-terminal amino acids of domain 1." According to the Examiner, it was not clear to which 15 N-terminal amino acids these claims referred. Claim 1 has been amended to recite that the 15 N-terminal amino acids refers to the first 15 N-terminal amino acids. Applicants submit that this claim rejection has been overcome and request withdrawal of this rejection.

Rejection of Claim 7 Under 35 U.S.C. 112, first paragraph

Claim 7 stands rejected under 35 U.S.C. 112 for allegedly lacking enablement. According to the Examiner, it is unclear if a cell line which produces an antibody having the exact structural and chemical identity of the claimed monoclonal antibody E4B9 are known and publicly available or can be reproducibly isolated without undue experimentation. Applicants have deposited a hybridoma cell line that produces monoclonal antibody E4B9. The cell line was deposited with the American Type Culture Collection under the terms of the Budapest Treaty. The specification has been amended to disclose the place of deposit and public accession number. All restrictions on the availability to the public of the deposited cell line will be irrevocably removed upon the granting of a patent and the deposit will be replaced if viable samples cannot be dispensed by the depository. According to the Examiner, deposit of the hybridoma producing E4B9 would satisfy the enablement requirement and therefore Applicants request withdrawal of this rejection.

Rejection of Claims 1-6 and 10-12 Under 35 U.S.C. 112, first paragraph

Claims 1-6 and 10-12 were rejected under 35 U.S.C. 112 for allegedly lacking enablement. According to the Examiner, the specification does not teach how to make any of the claimed antibodies and it would not be predictable to isolate an antibody specific for any of the recited epitopes with the claimed functional properties. Applicants traverse this rejection.

The present claims are directed to antibodies that recognize a specific epitope within a well-defined antigen. The epitope recognized by the antibodies recited in the claims lies within the first 15 N-terminal amino acids of domain 1 of VE-cadherin. The specification also teaches antibodies which specifically bind to the defined antigen and have the required property of inhibiting adherens function without significantly effecting paracellular permeability *in vitro*.

The general knowledge in the art is such that antibodies are structurally well-characterized. The level of skill in the art at the time of filing the present application was such that the production of antibodies against a well-characterized antigen was conventional. Moreover, the specification teaches, through example, an assay to determine the ability to obtain antibodies to inhibit adherens function and to determine

the effect on paracellular permeability *in vitro*. Thus, the specification provides sufficient guidance to enable the skilled practitioner to obtain and identify the spectrum of antibodies that bind to one of the three specific peptide antigens or to a site within the first 15 N-terminal amino acids of domain 1 of VE-cadherin as set forth in the claims.

Rejection of Claims 1-7 Under 35 U.S.C. 102(b)

Claims 1-7 stand rejected as being allegedly anticipated by an abstract from R & D Focus Drug News, November 17, 1997 from IMSDRUGNEWS database. Applicants traverse this rejection. According to the Examiner, the abstract refers to a highly specific monoclonal antibody antagonist E4B9 of VE-cadherin 2 that is claimed in Claim 7. This cited abstract, however, is simply a news update stating that ImClone Systems has initiated a screening program for the identification of a monoclonal antibody antagonist of VE-cadherin-2 and does nothing more than list "E4B9" in the "Descriptors" section at the end of the text of the abstract. There is absolutely no other description of the E4B9 antibody. As the Examiner is well-aware, "the disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; **mere naming or description of the subject matter is insufficient**, if it cannot be produced without undue experimentation." *Elan Pharm., Inc. v. Mayo Foundation for Medical and Education Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003) (*emphasis added*). The cited abstract does not describe the specific epitope to which E4B9 binds, a cell line that produces E4B9, or any other description of how to produce E4B9. As such, the cited abstract does not provide sufficient guidance to enable one skilled in the art to produce E4B9 and does not anticipate claims 1-7. Applicants request withdrawal of this rejection.

CONCLUSION

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees required in connection with the filing of this response, are hereby petitioned under 37 C.F.R. § 1.136(a), and the

Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,

KENYON & KENYON

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